DEPARTMENT OF HEALTH AND HUMAN SERVICES

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Certifier R. LEDESMA

Food and Drug Administration

[Docket No. 02D–0307]

Draft Guidance for Industry on Potassium Chloride Modified-Release Tablets and Capsules: In Vivo Bioequivalence and In Vitro Dissolution Testing, Revision; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration is announcing the availability of a revised draft guidance for industry entitled "Potassium Chloride Modified-Release Tablets and Capsules: In Vivo Bioequivalence and In Vitro Dissolution Testing." This draft guidance document provides recommendations to sponsors of abbreviated new drug applications (ANDAs) on the design of bioequivalence studies for modified-release dosage forms of potassium chloride.

DATES: Submit written or electronic comments on the draft guidance by [*insert date 45 days after date of publication in the* **Federal Register**]. General comments on agency guidance documents are welcome at any time.

ADDRESSES: Submit written requests for single copies of this draft guidance to the Division of Drug Information (HFD–240), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857. Send one self-addressed adhesive label to assist that office in processing your requests. Submit written comments on the draft guidance to the Dockets Management Branch (HFA–305), Food and Drug Administration, 5630 Fishers

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Lane, rm. 1061, Rockville, MD 20857. Submit electronic comments to http://www.fda.gov/dockets/ecomments. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT: Lizzie Sanchez, Center for Drug Evaluation and Research (HFD–650), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–5847.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a revised draft guidance for industry entitled "Potassium Chloride Modified-Release Tablets and Capsules: In Vivo Bioequivalence and In Vitro Dissolution Testing." This draft guidance is intended to provide information to sponsors of ANDAs on the design of bioequivalence studies for modified-release dosage forms of potassium chloride. A document entitled "Guidance for In Vivo Bioequivalence Study for Slow-Release Potassium Chloride Tablets/Capsules" was issued on May 15, 1987, and revised on June 6, 1994. The guidance is now being revised to incorporate current thinking on the bioequivalence requirements for potassium chloride modified-release products.

In the previous guidance, the agency recommended a three-way crossover study design comparing the reference product (RLD) to the generic product and to a solution of potassium chloride. The earlier guidance also recommended analysis of covariance (ANCOVA) for the pharmacokinetic parameters. The revised draft guidance provides recommendations for a two-way crossover study design comparing the generic product to the RLD. In addition, in the revision, the use of ANCOVA is no longer recommended. The

agency has found that the analysis of variance (ANOVA) with baseline correction is adequate for bioequivalence analysis of pharmacokinetic data obtained following oral administration of potassium chloride drug products. The recommendations for in vitro dissolution testing and the criteria for waivers of in vivo testing for lower strengths have been revised in accordance with the guidance entitled "Bioavailability and Bioequivalence Studies for Orally Administered Drug Products—General Considerations," issued in October 2000.

The agency is issuing this product-specific draft guidance because of special considerations for potassium chloride testing that are not covered in other agency guidances.

This revised draft guidance is being issued consistent with FDA's good guidance practices (21 CFR 10.115). The draft guidance, when finalized, will represent the agency's current thinking on studies to demonstrate the bioequivalence of potassium chloride modified-release tablets and capsules. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the applicable statutes and regulations.

II. Comments

Interested persons may submit to the Dockets Management Branch (see **ADDRESSES**) written or electronic comments on the draft guidance. Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. The draft guidance and received comments are available for public examination in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

III. Electronic Access

Persons with access to the Internet may obtain the document at either http://www.fda.gov/cder/guidance/index.htm or http://www.fda.gov/ohrms/dockets/default.htm.

Dated: 7/31/02

July 31, 2002.

Margaret M. Dotzel,
Associate Commissioner for Policy.

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